II. REMARKS

Formal Matters

Claims 1-17 are pending after entry of the amendments set forth herein.

Claims 1-17 were examined and were rejected.

Claims 5, 9, and 10 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as acquiescence to any objection or rejection of any claim. No new matter is added by these amendments.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Rejections under 35 U.S.C.§112, second paragraph

Claims 5 and 10 were rejected under 35 U.S.C.§112, second paragraph.

Claim 5

Claim 5 recites that the nucleic acid coding for the MSP-1 is reduced in its AT content compared to the wild-type sequence. The Office Action stated that the specification does not define "AT" nor does it include examples of sequences for comparison of the AT content. The Office Action stated that the claimed subject matter is not clearly defined. Applicants respectfully traverse the rejection.

The term "AT content" is an art-recognized term, and refers to the number of adenine-thymine base pairs relative to the number of guanine-cytosine base pairs in a nucleic acid. Thus, claim 5 is clear and need not be amended.

Furthermore, the instant specification incorporates by reference the disclosure of DE 19640817, which corresponds to U.S. Patent No. 6,933,130, and refers to "a nucleic acid sequence reduced in its AT content, as described in DE 19640817." Substitute Specification, paragraph 0043. U.S. Patent No. 6,933,130 ('130) states that AT-content means "the percentage amount of adenine-thymine base pairs compared to the guanine-cytosine base pairs." '130 patent, column 4, lines 65-67. DE 19640817 also corresponds to WO 98/14583, published on April 9, 1998.

As provided for under MPEP §608.01(p), and 37 C.F.R.§§1.57(f) and (g)(1) the Substitute Specification is amended to include the material incorporated by reference, i.e., to include the statement: "In the context of the present invention "AT-content" means the percentage amount of adenine-thymine base pairs compared to guanine-cytosine base pairs"; and to correct the incorporation by reference statement to use the root words "incorporate" and "reference." The material being inserted is the material previously incorporated by reference; as such, no new matter is added by the above-noted amendment to the specification.

Claim 10

Claim 10 recites that the signal sequence controls the GPI anchoring of the gene product. The Office Action stated that the specification does not define "GPI"; and stated that the claim does not particularly point out and distinctly claim the subject matter of the claimed invention.

GPI anchors are known in the art; those skilled in the art understand that "GPI" refers to a glycosylphosphatidylinositol anchor. Indeed, the instant specification states that the MSP-1 protein is present in erythrocytes, and anchored "via a glycosylphosphatidylinositol anchor." Substitute Specification, paragraph 0006. Throughout the specification, the MSP-1 protein is discussed in secreted or "anchored" form. See, e.g., Substitute Specification, paragraphs 0034, 0050, 0076, 0094, and 0098; and Table 1. Accordingly, the meaning of "GPI" is clear.

Nevertheless, in the interest of expediting prosecution, claim 10 is amended to recite "glycosylphosphatidylinositol."

Conclusion as to the rejections under 35 U.S.C. §112, second paragraph

Applicants submit that the rejection of claims 5 and 10 under 35 U.S.C. §112, second paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C.§112, first paragraph

Claims 1-17 were rejected under 35 U.S.C.§112, first paragraph, as allegedly lacking written description.

The Office Action stated that the present claims encompass numerous species that are not described. The Office Action stated that there is substantial variability among these species. The Office

Action stated that Applicants' disclosure is limited to the full-length MSP-1 proteins and to specific fragments designated p83, p30, p33, p19, and p42. The Office Action stated that there is no disclosure of any of the other claimed fragments or muteins and no guidance as to where to make mutations in either the full-length protein or any of the recited fragments. Applicants respectfully traverse the rejection.

The standard for determining compliance with the written description requirement is whether the "specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed." Essentially, the specification must clearly allow persons of ordinary skill in the art to recognize that they invented what is claimed.

The instant specification and claims comply with the written description requirement.

The instant specification, and thus the instant claims, are in compliance with the written description requirement of 35 U.S.C.§112, first paragraph. The instant specification describes an adequate number of nucleic acids encoding the recited MSP-1 protein. Furthermore, nucleic acids encoding *P. falciparum* MSP-1 proteins, fragments, and muteins were known in the art as of the October 23, 2002 priority date of the instant application.

The instant application identifies GenBank sources of MSP-1 amino acid sequences. Substitute Specification, paragraph 0042. As discussed in more detail below, the Federal Circuit has found that when the prior art includes the sequence information, precedent does not set a *per se* rule that the sequence information be provided afresh.

The instant application also incorporates by reference DE 19640817, which published as WO 98/14583 on April 9, 1998, and which discloses a number of *P. falciparum* MSP-1 sequences. See, e.g., U.S. Patent No. 6,933,130, which corresponds to WO 98/14583. Again, as discussed above, and as discussed further below, the Federal Circuit has found that when the prior art includes the sequence information, precedent does not set a *per se* rule that the sequence information be provided afresh.

It is noted that the term "mutein" is an art-recognized term referring to a protein arising as a result of a mutation. Those skilled in the art, given the ample description in the literature of various *P. falciparum* MSP-1 sequences, along with the description in the instant application and in DE19640817,

would recognize that Applicants were in possession of the instant invention as claimed.

The Federal Circuit's decisions in Capon and in Falkner are relevant to the instant claims.

The Federal Circuit's decision in *Capon v. Eshhar* (76 USPQ2d 1078 (CAFC 2005); "*Capon*") (Exhibit 1) and in *Falkner v. Inglis* (79 USPQ2d 1001 (CAFC 2006); "*Falkner*"; Exhibit 2) are relevant to the instant case.

Capon involved an interference between two parties claiming a chimeric DNA encoding a chimeric single-chain antibody. The parties argued that there was no need to know the structure of the DNA segments to make the claimed chimeric DNAs, because the structure of these components were already known, and methods for identifying, obtaining, and linking DNA segments were known. Despite this showing, the Board of Patent Appeals and Interferences (the "Board") found that neither party's specification met the written description requirement of 35 U.S.C.§112, first paragraph. The Board stated that:

> Their specifications do not satisfy the written description requirement because persons having ordinary skill in the art would not have been able to visualize and recognize the identity of the claimed genetic materials without considering additional knowledge in the art, performing additional experimentation, and testing to confirm results.[1]

The Federal Circuit reversed, finding that the Board "erred in refusing to consider the state of the scientific knowledge".[2] The court in *Capon* stated:

> The Board's rule that the nucleotide sequences of the chimeric genes must be fully presented, although the nucleotide sequences of the component DNA are known, is an inappropriate generalization. When the prior art includes the nucleotide information, precedent does not set a *per se* rule that the information must be determined afresh.[3]

and

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[1] *Capon* at page 9 (citing Board opinion).

[2] *Capon* at page 14.

[3] *Capon* at page 15.

> The "written description" requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution... The chimeric genes here at issue are prepared from known DNA sequences of known function....The Board erred in holding that the specifications do not meet the written description requirement because they do not reiterate the structure or formula or chemical name for the nucleotide sequences of the claimed chimeric genes.[4]

The instant Office Action raises issues similar to those raised by the Board and addressed by the Federal Circuit in *Capon*. The claimed invention recites recombinant MVA virus that includes nucleic acids encoding *P. falciparum* MSP-1 protein. Various nucleic acids encoding *P. falciparum* MSP-1 protein were known in the art as of the October 23, 2002 priority date. Accordingly, as in *Capon*, the Office should find that applicants' specification fulfills the written description requirement under §112, first paragraph with respect to the claimed invention.

The Office Action asserts that: 1) the present claims encompass numerous species that are not described; 2) there is substantial variability among these species; 3) Applicants' disclosure is limited to the full-length MSP-1 proteins and to specific fragments designated p83, p30, p33, p19, and p42; and 4) there is no disclosure of any of the other claimed fragments or muteins and no guidance as to where to make mutations in either the full-length protein or any of the recited fragments. However, as established by the court in *Capon*, where the level of skill in the art is such that the claimed invention includes the use of known nucleic acids encoding known proteins, the written description requirement does not require determining this information "afresh."

As discussed above, given the description in the literature of various *P. falciparum* MSP-1 sequences, along with the description in the instant application and in DE19640817, those skilled in the art would recognize that Applicants were in possession of the instant invention as claimed.

In *Capon*, the Federal Circuit noted that in *Lilly*, which involved claims to a vertebrate cDNA encoding insulin, the cDNA for human insulin *had never been characterized*. This was not the case in *Capon*, in which there was ample information available in the art. Just as in *Capon*, the present

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[4] *Capon* at page 15.

invention does ***not*** involve the situation in *Lilly*, which involved claims to a novel gene. In short, the *Lilly* decision simply does not apply to the instant case. Instead, the facts of *Capon* are more similar to those of the instant case. Accordingly, the Office should find, as did the Federal Circuit in *Capon*, that the specification satisfies the written description requirement of 35 U.S.C.§112, first paragraph for the claimed invention.

In *Falkner*, the Federal Circuit followed the *Capon* decision, and reiterated the fact that there is no per se rule that sequences provided in the prior art need be provided afresh in a patent application. *Falkner* is an appeal from a decision of the Board of Patent Appeals and Interferences ("Board") in an interference declared between a U.S. patent issued to Falkner and a U.S. application to Inglis. The Board found that the Inglis patent complied with the written description requirement; and the Federal Circuit agreed.

The Federal Circuit in *Falkner* stated:

> However, it is the binding precedent of this court that *Eli Lilly* does *not* set forth a *per se* rule that whenever a claim limitation is directed to a macromolecular sequence, the specification must always recite the gene or sequence, regardless of whether it is known in the prior art. *See Capon*, 418 F.3d at 1357 ("None of the cases to which the Board attributes the requirement of total DNA re-analysis, i.e., *Regents v. Lilly*, *Fiers v. Revel*, *Amgen*, or *Enzo Biochem*, require a re-description of what was already known."). Thus, "[w]hen the prior art includes the nucleotide information, precedent does not set a *per se* rule that the information must be determined afresh." *Id.* at 1358. Rather, we explained that:
>
> The descriptive text needed to meet these requirements varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence. The law must be applied to each invention that enters the patent process, for each patented advance is novel in relation to the state of the science. Since the law is applied to each invention in view of the state of relevant knowledge, its application will vary with differences in the state of knowledge in the field and differences in the predictability of the science. *Id.* at 1357.
>
> **Indeed, a requirement that patentees recite known DNA structures, if one existed, would serve no goal of the written description requirement.** It would neither enforce the quid pro quo between the patentee and the public by forcing the disclosure of new information, nor would it be necessary to demonstrate to a person of ordinary skill in the art that the patentee was in possession of the claimed invention. As we stated in *Capon*, "[t]he 'written description' requirement states that the patentee must describe the invention; it does not state that every invention must be

> described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution." *Id.* at 1358. Indeed, the forced recitation of known sequences in patent disclosures would only add unnecessary bulk to the specification. Accordingly we hold that where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences (here "essential genes"), satisfaction of the written description requirement does not require either the recitation or incorporation by reference (where permitted) of such genes and sequences. (emphasis added)

The Office should find, as did the Federal Circuit in *Capon* and in *Falkner*, that the specification satisfies the written description requirement of 35 U.S.C.§112, first paragraph for the claimed invention.

Conclusion as to the rejection under 35 U.S.C.§112, first paragraph

Applicants submit that the rejection of claims 1-17 under 35 U.S.C. §112, first paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C.§102(b)

Claims 1, 3, 4, 6, 7, and 10-17 were rejected under 35 U.S.C.§102(b) as allegedly anticipated by Yang et al. ((1997) *Vaccine* 15:1303-1313; "Yang").

The Office Action stated that Yang teaches a recombinant vaccinia virus encoding a *Plasmodium falciparum* merozoite surface antigen (MSA1). The Office Action stated that a highly attenuated strain of vaccinia virus, Modified Vaccinia Ankara (MVA) was developed as an expression vector and shown to be equivalent to replication competent vaccinia virus in several vaccine models. Applicants respectfully traverse the rejection.

It is basic patent law that in order to anticipate a claim, a reference must teach each and every element of the claim. A claim is anticipated only if each and every element as set forth in the claim is found in a single prior art reference. *Verdegaal Bros. v. Union Oil of California*, 2USPQ2d 1051, 1053 (Fed. Cir. 1987).

Yang does not teach each and every element of the instant claims. Yang discusses a recombinant vaccinia virus that comprises sequences encoding various C-terminal fragments of *P. falciparum* MSA1. While Yang states that MVA "has been developed as an expression vector and shown to be equivalent to replication competent vaccinia virus in several vaccine models," Yang does not disclose or suggest a MVA virus comprising a nucleic acid encoding a *P. falciparum* MSP-1 protein. Accordingly, Yang does not teach each and every element of the instant invention as claimed. As such, Yang cannot anticipate any of claims 1, 3, 4, 6, 7, and 10-17.

Conclusion as to the rejection under 35 U.S.C.§102(b)

Applicants submit that the rejection of claims 1, 3, 4, 6, 7, and 10-17 under 35 U.S.C. §102(b) has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C.§103(a)

Claims 1-4 and 6-17 were rejected under 35 U.S.C.§103(a) as allegedly unpatentable over Yang in view of McConkey et al. ((June 2003) *Nat. Medicine* 9:729-735; "McConkey").

McConkey is not available as prior art to the instant application.

McConkey is not available as prior art to the instant application under 35 U.S.C.§102(a). A printed publication is available as prior art under 35 U.S.C.§102(a), if the printed publication was published before the invention by applicant. McConkey was published in June, 2003, with electronic publication on May 25, 2003. The instant application claims priority to DE 10249390.1, which was filed on October 23, 2002. As provided for under 35 U.S.C.§119(a) and §365, the instant application is entitled to the October 23, 2002 priority date. McConkey published on May 25, 2003, which is later than the October 23, 2002 priority date of the instant application. Accordingly, McConkey is not available as prior art to the instant application under 35 U.S.C.§102(a).

McConkey is not available as prior art to the instant application under 35 U.S.C.§102(b). As provided for under 35 U.S.C. 363, an international application designating the United States has the effect, from its international filing date, of a national application for patent regularly filed in the U.S. Patent Office. The instant application is a filing under 35 U.S.C.§371 of WO 2004/038024, which

designated the U.S. and which has an international filing date of September 26, 2003. McConkey published on May 25, 2003, which is less than one year before September 26, 2003. Accordingly, McConkey is not available as prior art to the instant application under 35 U.S.C.§102(b).

The Office Action stated that Yang does not teach that the recombinant vaccinia virus MSP-1 protein is from the 3D7 or FCB1 isolate. The Office Action stated that McConkey teaches a recombinant MVA vaccine for protection against *Plasmodium falciparum* from the 3D-7 strain. The Office Action concluded that it would have been obvious to use MVA and the 3D7 strain of *Plasmodium faciparum* for a vaccine against malaria. Applicants respectfully traverse the rejection.

As explained above, Yang does not teach each and every element of the instant invention as claimed. Furthermore, as the Office Action acknowledged, Yang does not teach that the recombinant vaccinia virus MSP-1 protein is from the 3D7 or FCB1 isolate. As explained above, McConkey is not available as prior art to the instant application. Yang alone cannot render any of instant claims 1-4 and 6-17 obvious.

Conclusion as to the rejection under 35 U.S.C.§103(a)

Applicants submit that the rejection of claims 1-4 and 6-17 under 35 U.S.C. §103(a) has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number GRUE-004.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: Sept. 18, 2006

By: _____
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United States Court of Appeals for the Federal Circuit

03-1480, -1481
(Interference No. 103,887)

DANIEL J. CAPON, ARTHUR WEISS, BRIAN A. IRVING, MARGO R. ROBERTS, and KRISZTINA ZSEBO,

Appellants,

v.

ZELIG ESHHAR, DANIEL SCHINDLER, TOVA WAKS, and GIDEON GROSS,

Cross-Appellants,

v.

JON DUDAS, Director of the Patent and Trademark Office,

Intervenor.

Steven B. Kelber, Piper Rudnick, LLP, of Washington, DC, argued for appellants.

Roger L. Browdy, Browdy and Neimark, P.L.L.C., of Washington, DC, argued for cross-appellants.

Mary L. Kelly, Associate Solicitor, Office of the Solicitor, United States Patent and Trademark Office, of Arlington, Virginia, argued for intervenor. With her on the brief were John M. Whealan, Solicitor and Stephen Walsh, Associate Solicitor.

Appealed from: United States Patent and Trademark Office Board of Patent Appeals and Interferences

(Bd. Pat. App. & Interf. Mar. 26, 2003). The Board dissolved the interference and cancelled all of the claims of both parties corresponding to the interference count. With this ruling, the Board terminated the proceeding and did not reach the question of priority of invention. We conclude that the Board erred in its application of the law of written description. The decision is vacated and the case is remanded to the Board for further proceedings.

BACKGROUND

Daniel J. Capon, Arthur Weiss, Brian A. Irving, Margo R. Roberts, and Krisztina Zsebo (collectively "Capon") and Zelig Eshhar, Daniel Schindler, Tova Waks, and Gideon Gross (collectively "Eshhar") were the parties to an interference proceeding between Capon's United States Patent No. 6,407,221 ("the '221 patent") entitled "Chimeric Chains for Receptor-Associated Signal Transduction Pathways" and Eshhar's patent application Serial No. 08/084,994 ("the '994 application") entitled "Chimeric Receptor Genes and Cells Transformed Therewith." Capon's Patent No. 5,359,046 ("the '046 patent"), parent of the '221 patent, was also included in the interference but was held expired for non-payment of a maintenance fee. The PTO included the '046 patent in its decision and in its argument of this appeal.[1]

A patent interference is an administrative proceeding pursuant to 35 U.S.C. §§102(g) and 135(a), conducted for the purpose of determining which of competing applicants is the first inventor of common subject matter. An interference is instituted after the separate

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1 Although Capon is designated as appellant and Eshhar as cross-appellant, both appealed the Board's decision. See Fed. R. App. P. 28(h). The Director of the PTO intervened to support the Board, and has fully participated in this appeal.

United States Court of Appeals for the Federal Circuit

03-1480, -1481
(Interference No. 103,887)

DANIEL J. CAPON, ARTHUR WEISS, BRIAN A. IRVING,
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Appellants,

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ZELIG ESHHAR, DANIEL SCHINDLER, TOVA WAKS,
and GIDEON GROSS,
Cross-Appellants,

v.

JON DUDAS,
Director of the Patent and Trademark Office,
Intervenor.

DECIDED: August 12, 2005

Before NEWMAN, MAYER,* and GAJARSA, Circuit Judges.

NEWMAN, Circuit Judge.

Both of the parties to a patent interference proceeding have appealed the decision of the Board of Patent Appeals and Interferences of the United States Patent and Trademark Office, wherein the Board held that the specification of neither party met the written description requirement of the patent statute. Capon v. Eshhar, Interf. No. 103,887

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* Haldane Robert Mayer vacated the position of Chief Judge on December 24, 2004.

patent applications have been examined and found to contain patentable subject matter. Capon's patents had been examined and had issued before this interference was instituted, and Eshhar's application had been examined and allowed but a patent had not yet issued.

During an interference proceeding the Board is authorized to determine not only priority of invention but also to redetermine patentability. 35 U.S.C. §6(b). The question of patentability of the claims of both parties was raised *sua sponte* by an administrative patent judge during the preliminary proceedings. Thereafter the Board conducted an *inter partes* proceeding limited to this question, receiving evidence and argument. The Board then invalidated all of the claims that had been designated as corresponding to the count of the interference, viz., all of the claims of the Capon '221 patent, claims 5-8 of the Capon '046 patent, and claims 1-7, 9-20, and 23 of the Eshhar '994 application.

In accordance with the Administrative Procedure Act, the law as interpreted and applied by the agency receives plenary review on appeal, and the agency's factual findings are reviewed to determine whether they were arbitrary, capricious, or unsupported by substantial evidence in the administrative record. See 5 U.S.C. §706(2); Dickinson v. Zurko, 527 U.S. 150, 164-65 (1999); In re Gartside, 203 F.3d 1305, 1315 (Fed. Cir. 2000).

The Invention

A chimeric gene is an artificial gene that combines segments of DNA in a way that does not occur in nature. The '221 patent and '994 application are directed to the production of chimeric genes designed to enhance the immune response by providing cells with specific cell-surface antibodies in a form that can penetrate diseased sites, such as solid tumors, that were not previously reachable. The parties explain that their invention is

a way of endowing immune cells with antibody-type specificity, by combining known antigen-binding-domain producing DNA and known lymphocyte-receptor-protein producing DNA into a unitary gene that can express a unitary polypeptide chain. Eshhar summarized the problem to which the invention is directed:

> Antigen-specific effector lymphocytes, such as tumor-specific T cells, are very rare, individual-specific, limited in their recognition spectrum and difficult to obtain against most malignancies. Antibodies, on the other hand, are readily obtainable, more easily derived, have wider spectrum and are not individual-specific. The major problem of applying specific antibodies for cancer immunotherapy lies in the inability of sufficient amounts of monoclonal antibodies (mAb) to reach large areas within solid tumors.

Technical Paper Explaining Eshhar's Invention, at 6.

The inventions of Capon and Eshhar are the chimeric DNA that encodes single-chain chimeric proteins for expression on the surface of cells of the immune system, plus expression vectors and cells transformed by the chimeric DNA. The experts for both parties explain that the invention combines selected DNA segments that are both endogenous and nonendogenous to a cell of the immune system, whereby the nonendogenous segment encodes the single-chain variable ("scFv") domain of an antibody, and the endogenous segment encodes cytoplasmic, transmembrane, and extracellular domains of a lymphocyte signaling protein. They explain that the scFv domain combines the heavy and light variable ("Fv") domains of a natural antibody, and thus has the same specificity as a natural antibody. Linking this single chain domain to a lymphocyte signaling protein creates a chimeric scFv-receptor ("scFvR") gene which, upon transfection into a cell of the immune system, combines the specificity of an antibody with the tissue penetration, cytokine production, and target-cell destruction capability of a lymphocyte.

The parties point to the therapeutic potential if tumors can be infiltrated with specifically designed immune cells of appropriate anti-tumor specificity.

The Eshhar Claims

The Board held unpatentable the following claims of Eshhar's '994 application; these were all of the '994 claims that had been designated as corresponding to the count of the interference. Eshhar's claim 1 was the designated count.

> 1. A chimeric gene comprising
>
> a first gene segment encoding a single-chain Fv domain (scFv) of a specific antibody and
>
> a second gene segment encoding partially or entirely the transmembrane and cytoplasmic, and optionally the extracellular, domains of an endogenous protein
>
> wherein said endogenous protein is expressed on the surface of cells of the immune system and triggers activation and/or proliferation of said cells,
>
> which chimeric gene, upon transfection to said cells of the immune system, expresses said scFv domain and said domains of said endogenous protein in one single chain on the surface of the transfected cells such that the transfected cells are triggered to activate and/or proliferate and have MHC nonrestricted antibody-type specificity when said expressed scFV domain binds to its antigen.
>
> 2. A chimeric gene according to claim 1 wherein the second gene segment further comprises partially or entirely the extracellular domain of said endogenous protein.
>
> 3. A chimeric gene according to claim 1 wherein the first gene segment encodes the scFv domain of an antibody against tumor cells.
>
> 4. A chimeric gene according to claim 1 wherein the first gene segment encodes the scFv domain of an antibody against virus infected cells.
>
> 5. A chimeric gene according to claim 4 wherein the virus is HIV.
>
> 6. A chimeric gene according to claim 1 wherein the second gene segment encodes a lymphocyte receptor chain.
>
> 7. A chimeric gene according to claim 6 wherein the second gene segment encodes a chain of the T cell receptor.

9. A chimeric gene according to claim 7 wherein the second gene segment encodes the α, β, γ, or δ chain of the antigen-specific T cell receptor.

10. A chimeric gene according to claim 1 wherein the second gene segment encodes a polypeptide of the TCR/CD3 complex.

11. A chimeric gene according to claim 10 wherein the second gene segment encodes the zeta or eta isoform chain.

12. A chimeric gene according to claim 1 wherein the second gene segment encodes a subunit of the Fc receptor or IL-2 receptor.

13. A chimeric gene according to claim 12 wherein the second gene segment encodes a common subunit of IgE and IgG binding Fc receptors.

14. A chimeric gene according to claim 13 wherein said subunit is the gamma subunit.

15. A chimeric gene according to claim 13 wherein the second gene segment encodes the CD16α chain of the FcγRIII or FcγRII.

16. A chimeric gene according to claim 12 wherein the second gene segment encodes the α or β subunit of the IL-2 receptor.

17. An expression vector comprising a chimeric gene according to claim 1.

18. A cell of the immune system endowed with antibody specificity transformed with an expression vector according to claim 17.

19. A cell of the immune system endowed with antibody specificity comprising a chimeric gene according to claim 1.

20. A cell if the immune system according to claim 19 selected from the group consisting of a natural killer cell, a lymphokine activated killer cell, a cytotoxic T cell, a helper T cell and a subtype thereof.

23. A chimeric gene according to claim 1 wherein said endogenous protein is a lymphocyte receptor chain, a polypeptide of the TCR/CD3 complex, or a subunit of the Fc or IL-2 receptor.

The Board did not discuss the claims separately, and held that the specification failed to satisfy the written description requirement as to all of these claims.

The Capon Claims

Claims 1-10, all of the claims of the '221 patent, were held unpatentable on written description grounds. Claims 1-6 are directed to the chimeric DNA, claims 7, 8, and 10 to the corresponding cell comprising the DNA, and claim 9 to the chimeric protein:

> 1. A chimeric DNA encoding a membrane bound protein, said chimeric DNA comprising in reading frame:
>
> DNA encoding a signal sequence which directs said membrane bound protein to the surface membrane;
>
> DNA encoding a non-MHC restricted extracellular binding domain which is obtained from a single chain antibody that binds specifically to at least one ligand, wherein said at least one ligand is a protein on the surface of a cell or a viral protein;
>
> DNA encoding a transmembrane domain which is obtained from a protein selected from the group consisting of CD4, CD8, immunoglobulin, the CD3 zeta chain, the CD3 gamma chain, the CD3 delta chain and the CD3 epsilon chain; and
>
> DNA encoding a cytoplasmic signal-transducing domain of a protein that activates an intracellular messenger system which is obtained from CD3 zeta,
>
> wherein said extracellular domain and said cytoplasmic domain are not naturally joined together, and said cytoplasmic domain is not naturally joined to an extracellular ligand-binding domain, and when said chimeric DNA is expressed as a membrane bound protein in a host cell under conditions suitable for expression, said membrane bound protein initiates signaling in said host cell when said extracellular domain binds said at least one ligand.
>
> 2. The DNA of claim 1, wherein said single-chain antibody recognizes an antigen selected from the group consisting of viral antigens and tumor cell associated antigens.
>
> 3. The DNA of claim 2 wherein said single-chain antibody is specific for the HIV env glycoprotein.
>
> 4. The DNA of claim 1, wherein said transmembrane domain is naturally joined to said cytoplasmic domain.
>
> 5. An expression cassette comprising a transcriptional initiation region, the DNA of claim 1 under the transcriptional control of said transcriptional initiation region, and a transcriptional termination region.

6. A retroviral RNA or DNA construct comprising the expression cassette of claim 5.

7. A cell comprising the DNA of claim 1.

8. The cell of claim 7, wherein said cell is a human cell.

9. A chimeric protein comprising in the N-terminal to C-terminal direction:

a non-MHC restricted extracellular binding domain which is obtained from a single chain antibody that binds specifically to at least one ligand, wherein said at least one ligand is a protein on the surface of a cell or a viral protein;

a transmembrane domain which is obtained from a protein selected from the group consisting CD4, CD8, immunoglobulin, the CD3 zeta chain, the CD3 gamma chain, the CD3 delta chain and the CD3 epsilon chain; and

a cytoplasmic signal-transducing domain of a protein that activates an intracellular messenger system which is obtained from CD3 zeta,

wherein said extracellular domain and said cytoplasmic domain are not naturally joined together, and said cytoplasmic domain is not naturally joined to an extracellular ligand-binding domain, and when said chimeric protein is expressed as a membrane bound protein in a host cell under conditions suitable for expression, said membrane bound protein initiates signaling in said host cell when said extracellular domain binds said at least one ligand.

10. A mammalian cell comprising as a surface membrane protein, the protein of claim 9.

In addition, claims 5, 6, 7, and 8 of Capon's '046 patent were held unpatentable. These claims are directed to chimeric DNA sequences where the encoded extracellular domain is a single-chain antibody containing ligand binding activity.

The Board Decision

The Board presumed enablement by the specifications of the '221 patent and '994 application of the full scope of their claims, and based its decision solely on the ground of

failure of written description. The Board held that neither party's specification provides the requisite description of the full scope of the chimeric DNA or encoded proteins, by reference to knowledge in the art of the "structure, formula, chemical name, or physical properties" of the DNA or the proteins. In the Board's words:

> We are led by controlling precedent to understand that the full scope of novel chimeric DNA the parties claim is not described in their specifications under 35 U.S.C. §112, first paragraph, by reference to contemporary and/or prior knowledge in the art of the structure, formula, chemical name, or physical properties of many protein domains, and/or DNA sequences which encode many protein domains, which comprise single-chain proteins and/or DNA constructs made in accordance with the plans, schemes, and examples thereof the parties disclose.

Bd. op. at 4. As controlling precedent the Board cited Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559 (Fed. Cir. 1997); Fiers v. Revel Co., 984 F.2d 1164 (Fed. Cir. 1993); Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200 (Fed. Cir. 1991); and Enzo Biochem, Inc. v. Gen-Probe, Inc., 296 F.3d 1316 (Fed. Cir. 2002). The Board summarized its holding as follows:

> Here, both Eshhar and Capon claim novel genetic material described in terms of the functional characteristics of the protein it encodes. Their specifications do not satisfy the written description requirement because persons having ordinary skill in the art would not have been able to visualize and recognize the identity of the claimed genetic material without considering additional knowledge in the art, performing additional experimentation, and testing to confirm results.

Bd. op. at 89.

DISCUSSION

Eshhar and Capon challenge both the Board's interpretation of precedent and the Board's ruling that their descriptions are inadequate. Both parties explain that their

chimeric genes are produced by selecting and combining known heavy- and light-chain immune-related DNA segments, using known DNA-linking procedures. The specifications of both parties describe procedures for identifying and obtaining the desired immune-related DNA segments and linking them into the desired chimeric genes. Both parties point to their specific examples of chimeric DNA prepared using identified known procedures, along with citation to the scientific literature as to every step of the preparative method.

The parties presented expert witnesses who placed the invention in the context of prior knowledge and explained how the descriptive text would be understood by persons of skill in the field of the invention. The witnesses explained that the principle of forming chimeric genes from selected segments of DNA was known, as well as their methods of identifying, selecting, and combining the desired segments of DNA. Dr. Eshhar presented an expert statement wherein he explained that the prior art contains extensive knowledge of the nucleotide structure of the various immune-related segments of DNA; he stated that over 785 mouse antibody DNA light chains and 1,327 mouse antibody DNA heavy chains were known and published as early as 1991. Similarly Capon's expert Dr. Desiderio discussed the prior art, also citing scientific literature:

> The linker sequences disclosed in the '221 patent (col. 24, lines 4 and 43) used to artificially join a heavy and light chain nucleic acid sequence and permit functional association of the two ligand binding regions were published by 1990, as were the methods for obtaining the mature sequences of the desired heavy and light chains for constructing a SAb (Exhibit 47, Batra et al., J., Biol. Chem., 1990; Exhibit 48, Bird et al., Science, 1988; Exhibit 50, Huston et al., PNAS, 1988; Exhibit 51, Chaudhary, PNAS, 1990, Exhibit 56, Morrison et al., Science, 1985; Exhibit 53, Sharon et al., Nature 1984).

Desiderio declaration at 4 ¶11.

Both parties stated that persons experienced in this field would readily know the structure of a chimeric gene made of a first segment of DNA encoding the single-chain variable region of an antibody, and a second segment of DNA encoding an endogenous protein. They testified that re-analysis to confirm these structures would not be needed in order to know the DNA structure of the chimeric gene, and that the Board's requirement that the specification must reproduce the "structure, formula, chemical name, or physical properties" of these DNA combinations had been overtaken by the state of the science. They stated that where the structure and properties of the DNA components were known, reanalysis was not required.

Eshhar's specification contains the nucleotide sequences of sixteen different receptor primers and four different scFv primers from which chimeric genes encoding scFvR may be obtained, while Capon's specification cites literature sources of such information. Eshhar's specification shows the production of chimeric genes encoding scFvR using primers, as listed in Eshhar's Table I. Capon stated that natural genes are isolated and joined using conventional methods, such as the polymerase chain reaction or cloning by primer repair. Capon, like Eshhar, discussed various known procedures for identifying, obtaining, and linking DNA segments, accompanied by experimental examples. The Board did not dispute that persons in this field of science could determine the structure or formula of the linked DNA from the known structure or formula of the components.

The Board stated that "controlling precedent" required inclusion in the specification of the complete nucleotide sequence of "at least one" chimeric gene. Bd. op. at 4. The Board also objected that the claims were broader than the specific examples. Eshhar and

Capon each responds by pointing to the scientific completeness and depth of their descriptive texts, as well as to their illustrative examples. The Board did not relate any of the claims, broad or narrow, to the examples, but invalidated all of the claims without analysis of their scope and the relation of claim scope to the details of the specifications.

Eshhar and Capon both argue that they have set forth an invention whose scope is fully and fairly described, for the nucleotide sequences of the DNA in chimeric combination is readily understood to contain the nucleotide sequences of the DNA components. Eshhar points to the general and specific description in his specification of known immune-related DNA segments, including the examples of their linking. Capon points similarly to his description of selecting DNA segments that are known to express immune-related proteins, and stresses the existing knowledge of these segments and their nucleotide sequences, as well as the known procedures for selecting and combining DNA segments, as cited in the specification.

Both parties argue that the Board misconstrued precedent, and that precedent does not establish a *per se* rule requiring nucleotide-by-nucleotide re-analysis when the structure of the component DNA segments is already known, or readily determined by known procedures.

The Statutory Requirement

The required content of the patent specification is set forth in Section 112 of Title 35:

> §112 ¶1. The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full,

> clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The "written description" requirement implements the principle that a patent must describe the technology that is sought to be patented; the requirement serves both to satisfy the inventor's obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the patentee was in possession of the invention that is claimed. See Enzo Biochem, 296 F.3d at 1330 (the written description requirement "is the quid pro quo of the patent system; the public must receive meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time"); Reiffin v. Microsoft Corp., 214 F.3d 1342, 1345-46 (Fed. Cir. 2000) (the purpose of the written description requirement "is to ensure that the scope of the right to exclude . . . does not overreach the scope of the inventor's contribution to the field of art as described in the patent specification"); In re Barker, 559 F.2d 588, 592 n.4 (CCPA 1977) (the goal of the written description requirement is "to clearly convey the information that an applicant has invented the subject matter which is claimed"). The written description requirement thus satisfies the policy premises of the law, whereby the inventor's technical/scientific advance is added to the body of knowledge, as consideration for the grant of patent exclusivity.

The descriptive text needed to meet these requirements varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence. The law must be applied to each invention that enters the patent process, for each patented advance is novel in relation to the state of the science. Since the law is applied to each invention in view of the state of relevant knowledge, its application will vary

with differences in the state of knowledge in the field and differences in the predictability of the science.

For the chimeric genes of the Capon and Eshhar inventions, the law must take cognizance of the scientific facts. The Board erred in refusing to consider the state of the scientific knowledge, as explained by both parties, and in declining to consider the separate scope of each of the claims. None of the cases to which the Board attributes the requirement of total DNA re-analysis, i.e., Regents v. Lilly, Fiers v. Revel, Amgen, or Enzo Biochem, require a re-description of what was already known. In Lilly, 119 F.3d at 1567, the cDNA for human insulin had never been characterized. Similarly in Fiers, 984 F.2d at 1171, much of the DNA sought to be claimed was of unknown structure, whereby this court viewed the breadth of the claims as embracing a "wish" or research "plan." In Amgen, 927 F.2d at 1206, the court explained that a novel gene was not adequately characterized by its biological function alone because such a description would represent a mere "wish to know the identity" of the novel material. In Enzo Biochem, 296 F.3d at 1326, this court reaffirmed that deposit of a physical sample may replace words when description is beyond present scientific capability. In Amgen Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1332 (Fed. Cir. 2003) the court explained further that the written description requirement may be satisfied "if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." These evolving principles were applied in Noelle v. Lederman, 355 F.3d 1343, 1349 (Fed. Cir. 2004), where the court affirmed that the human antibody there at issue was not adequately described by the structure and function of the mouse antigen; and in University of Rochester v. G.D. Searle & Co., 358 F.3d 916, 925-26 (Fed.

Cir. 2004), where the court affirmed that the description of the COX-2 enzyme did not serve to describe unknown compounds capable of selectively inhibiting the enzyme.

The "written description" requirement must be applied in the context of the particular invention and the state of the knowledge. The Board's rule that the nucleotide sequences of the chimeric genes must be fully presented, although the nucleotide sequences of the component DNA are known, is an inappropriate generalization. When the prior art includes the nucleotide information, precedent does not set a *per se* rule that the information must be determined afresh. Both parties state that a person experienced in the field of this invention would know that these known DNA segments would retain their DNA sequences when linked by known methods. Both parties explain that their invention is not in discovering which DNA segments are related to the immune response, for that is in the prior art, but in the novel combination of the DNA segments to achieve a novel result.

The "written description" requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution. Both Eshhar and Capon explain that this invention does not concern the discovery of gene function or structure, as in Lilly. The chimeric genes here at issue are prepared from known DNA sequences of known function. The Board's requirement that these sequences must be analyzed and reported in the specification does not add descriptive substance. The Board erred in holding that the specifications do not meet the written description requirement because they do not reiterate the structure or formula or chemical name for the nucleotide sequences of the claimed chimeric genes.

Claim Scope

There remains the question of whether the specifications adequately support the breadth of all of the claims that are presented. The Director argues that it cannot be known whether all of the permutations and combinations covered by the claims will be effective for the intended purpose, and that the claims are too broad because they may include inoperative species. The inventors say that they have provided an adequate description and exemplification of their invention as would be understood by persons in the field of the invention. They state that biological properties typically vary, and that their specifications provide for evaluation of the effectiveness of their chimeric combinations.

It is well recognized that in the "unpredictable" fields of science, it is appropriate to recognize the variability in the science in determining the scope of the coverage to which the inventor is entitled. Such a decision usually focuses on the exemplification in the specification. See, e.g., Enzo Biochem, 296 F.3d at 1327-28 (remanding for district court to determine "[w]hether the disclosure provided by the three deposits in this case, coupled with the skill of the art, describes the genera of claims 1-3 and 5"); Lilly, 119 F.3d at 1569 (genus not described where "a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus" had not been provided); In re Gostelli, 872 F.2d 1008, 1012 (Fed. Cir. 1989) (two chemical compounds were insufficient description of subgenus); In re Smith, 458 F.2d 1389, 1394-95 (CCPA 1972) (disclosure of genus and one species was not sufficient description of intermediate subgenus); In re Grimme, 274 F.2d 949, 952 (CCPA 1960) (disclosure of single example and statement of scope sufficient disclosure of subgenus).

Precedent illustrates that the determination of what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing

knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter. See, e.g., In re Wallach, 378 F.3d 1330, 1333-34 (Fed. Cir. 2004) (an amino acid sequence supports "the entire genus of DNA sequences" that can encode the amino acid sequence because "the state of the art has developed" such that it is a routine matter to convert one to the other); University of Rochester, 358 F.3d at 925 (considering whether the patent disclosed the compounds necessary to practice the claimed method, given the state of technology); Singh v. Brake, 317 F.3d 1334, 1343 (Fed. Cir. 2002) (affirming adequacy of disclosure by distinguishing precedent in which the selection of a particular species within the claimed genus had involved "highly unpredictable results").

It is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention. See In re Angstadt, 537 F.2d 498, 504 (CCPA 1976) ("The examples, both operative and inoperative, are the best guidance this art permits, as far as we can conclude from the record"). While the Board is correct that a generic invention requires adequate support, the sufficiency of the support must be determined in the particular case. Both Eshhar and Capon present not only general teachings of how to select and recombine the DNA, but also specific examples of the production of specified chimeric genes. For example, Eshhar points out that in Example 1 of his specification the FcRγ chain was used, which chain was amplified from a human cDNA clone, using the procedure of Kuster, H. et al., J. Biol. Chem., 265:6448-6451 (1990), which is cited in the specification and reports the complete sequence of the FcRγ

chain. Eshhar's Example 1 also explains the source of the genes that provide the heavy and light chains of the single chain antibody, citing the PhD thesis of Gideon Gross, a co-inventor, which cites a reference providing the complete sequence of the Sp6 light chain gene used to construct the single-chain antibody. Eshhar states that the structure of the Sp6 heavy chain antibody was well known to those of skill in the art and readily accessible on the internet in a database as entry EMBL:MMSP6718. Example 5 at page 54 of the Eshhar specification cites Ravetch et al., J. Exp. Med., 170:481-497 (1989) for the method of producing the CD16α DNA clone that was PCR amplified; this reference published the complete DNA sequence of the CD16α chain, as discussed in paragraph 43 of the Eshhar Declaration. Example 3 of the Eshhar specification uses the DNA of the monoclonal anti-HER2 antibody and states that the N29 hybridoma that produces this antibody was deposited with the Collection Nationale de Cultures de Microorganismes, Institut Pasteur, Paris, on August 19, 1992, under Deposit No. CNCM I-1262. It is incorrect to criticize the methods, examples, and referenced prior art of the Eshhar specification as but "a few PCR primers and probes," as does the Director's brief.

Capon's Example 3 provides a detailed description of the creation and expression of single chain antibody fused with T-cell receptor zeta chain, referring to published vectors and procedures. Capon, like Eshhar, describes gene segments and their ligation to form chimeric genes. Although Capon includes fewer specific examples in his specification than does Eshhar, both parties used standard systems of description and identification, as well as known procedures for selecting, isolating, and linking known DNA segments. Indeed, the Board's repeated observation that the full scope of all of the claims appears to be "enabled" cannot be reconciled with the Board's objection that only a "general plan" to

combine unidentified DNA is presented. See In re Wands, 858 F.2d 731, 736-37 (Fed. Cir. 1988) (experimentation to practice invention must not be "undue" for invention to be considered enabled).

The PTO points out that for biochemical processes relating to gene modification, protein expression, and immune response, success is not assured. However, generic inventions are not thereby invalid. Precedent distinguishes among generic inventions that are adequately supported, those that are merely a "wish" or "plan," the words of Fiers v. Revel, 984 F.2d at 1171, and those in between, as illustrated by Noelle v. Lederman, 355 F.3d at 1350; the facts of the specific case must be evaluated. The Board did not discuss the generic concept that both Capon and Eshhar described -- the concept of selecting and combining a gene sequence encoding the variable domain of an antibody and a sequence encoding a lymphocyte activation protein, into a single DNA sequence which, upon expression, allows for immune responses that do not occur in nature. The record does not show this concept to be in the prior art, and includes experimental verification as well as potential variability in the concept.

Whether the inventors demonstrated sufficient generality to support the scope of some or all of their claims, must be determined claim by claim. The Board did not discuss the evidence with respect to the generality of the invention and the significance of the specific examples, instead simply rejecting all the claims for lack of a complete chimeric DNA sequence. As we have discussed, that reasoning is inapt for this case. The Board's position that the patents at issue were merely an "invitation to experiment" did not distinguish among the parties' broad and narrow claims, and further concerns enablement more than written description. See Adang v. Fischhoff, 286 F.3d 1346, 1355 (Fed. Cir.

2002) (enablement involves assessment of whether one of skill in the art could make and use the invention without undue experimentation); In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993) (same). Although the legal criteria of enablement and written description are related and are often met by the same disclosure, they serve discrete legal requirements.

The predictability or unpredictability of the science is relevant to deciding how much experimental support is required to adequately describe the scope of an invention. Our predecessor court summarized in In re Storrs, 245 F.2d 474, 478 (CCPA 1957) that "[i]t must be borne in mind that, while it is necessary that an applicant for a patent give to the public a complete and adequate disclosure in return for the patent grant, the certainty required of the disclosure is not greater than that which is reasonable, having due regard to the subject matter involved." This aspect may warrant exploration on remand.

In summary, the Board erred in ruling that §112 imposes a *per se* rule requiring recitation in the specification of the nucleotide sequence of claimed DNA, when that sequence is already known in the field. However, the Board did not explore the support for each of the claims of both parties, in view of the specific examples and general teachings in the specifications and the known science, with application of precedent guiding review of the scope of claims.

We remand for appropriate further proceedings.

VACATED AND REMANDED

United States Court of Appeals for the Federal Circuit

05-1324
(Interference No. 105,187)

FALKO-GUNTER FALKNER, GEORG HOLZER, and FRIEDRICH DORNER,

Appellants,

v.

STEPHEN C. INGLIS, MICHAEL E.G. BOURSNELL, and ANTHONY C. MINSON,

Appellees.

John P. Isacson, Heller Ehrman LLP, of Washington, DC, argued for appellants. With him on the brief was Paul M. Booth.

Robert G. McMorrow, Jr., Connolly Bove Lodge & Hutz LLP, of Wilmington, Delaware, argued for appellee.

Appealed from: United States Patent and Trademark Office, Board of Patent Appeals and Interferences

United States Court of Appeals for the Federal Circuit

05-1324
(Interference No. 105,187)

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v.

STEPHEN C. INGLIS, MICHAEL E.G. BOURSNELL, and ANTHONY C. MINSON,

Appellees.

DECIDED: May 26, 2006

Before GAJARSA, Circuit Judge, ARCHER, Senior Circuit Judge and DYK, Circuit Judge.

GAJARSA, Circuit Judge.

This is an appeal from a decision of the Board of Patent Appeals and Interferences ("Board") in Interference No. 105,187, declared on December 24, 2003, between Falkner *et al.*, U.S. Patent No. 5,770,212 ("the Falkner '212 patent") and Inglis *et al.*, U.S. Application Serial No. 08/459,040 ("the Inglis '040 application"). The Administrative Patent Judge (APJ) designated Inglis as the senior party. On December 29, 2004, the Board issued a final decision, holding that Falkner could not antedate Inglis' September 25, 1990 priority date, and entered judgment against Falkner on the

sole count of the interference. It ordered that Falkner was not entitled to claims 1-19 of the Falkner '212 patent. It further ordered that Inglis was entitled to claims 9, 10, 29 and 30 of the '040 application. Falkner filed a timely notice of appeal. This Court has jurisdiction pursuant to 28 U.S.C. § 1295(a)(4)(A) and 35 U.S.C. §§ 141 and 142. For the reasons discussed below, we affirm the judgment of the Board.

I. BACKGROUND

A. The Invention

Some vaccines against a virus (the "target virus") incorporate harmless fragments of the target virus's genetic material into a second virus, called a "viral vector." When a person is vaccinated, the viral vector produces harmless fragments of the target virus, ultimately conferring immunity against it. To prevent the viral vector from itself causing a harmful infection in the inoculee, it must be attenuated. Attenuation is achieved by deleting or inactivating one or more genes responsible for the vector's growth and infectiousness. However, because the vaccine is produced by essentially "growing" the vector virus (accompanied by its inserted target virus gene), attenuation makes it difficult to manufacture the vaccine. The traditional solution to this problem has been to inactivate genes known as "inessential" genes. With inessential genes inactivated, the viral vector is substantially less pathogenic. At the same time, because the vector virus can still fully reproduce itself, albeit more slowly, the vaccine can be produced in commercial quantities. However, the traditional approach carried a disadvantage, namely the risk that the vector virus, though attenuated, could still cause a harmful infection in the inoculee.

The inventors discovered a way of making vaccines safer by deleting or inactivating an essential, rather than an inessential, gene from the viral vector's genome, while at the same time solving the production problem by growing the vaccines in cells that were complementarily modified to produce the absent essential viral gene product "on behalf of" the vector virus. Thus, the modified vector virus could be readily grown in these complementarily-modified cells, but not in other cells, such as those of an inoculee.

This approach is applicable to many different kinds of vector viruses, e.g., adenoviruses, herpesviruses, poxviruses and retroviruses. The subject matter of this interference, however, is directed specifically to vaccines in which the vector virus is a poxvirus. For many vector viruses, there is a risk that vectors that have been attenuated in essential genes can "swap" genes with the host cell genome, thereby reacquiring their deleted genes and reverting to wild-type virus. This risk can be minimized through the use of viruses that are "cytoplasmic", meaning that they are unlikely to enter the cell nucleus. Because a cell's genes are located in the nucleus, cytoplasmic viruses such as poxvirus cannot swap genes with the cell genome and possibly revert to a virulent wild-type virus.

B. Defining the Count and Assigning Priority

The sole count of the interference was either "[a] vaccine according to Claim 1 of Falkner's 5,770,212 patent or a vaccine according to Claim 29 of Inglis' 08/459,040 application." Claim 29 of the Inglis '040 application reads:

> A vaccine comprising a pharmaceutically acceptable excipient and an effective immunizing amount of a mutant virus, wherein said mutant virus is a mutant poxvirus and has a genome which has an inactivating mutation in a viral gene, said viral gene being essential for the production of

> infectious new virus particles, wherein said mutant virus is able to cause production of infectious new virus particles in a complementing host cell gene expressing a gene which complements said essential viral gene, but is unable to cause production of infectious new virus particles when said mutant virus infects a host cell other than a complementing host cell; for prophylactic or therapeutic use in generating an immune response in a subject.

(emphasis added)

Claim 1 of the Falkner '212 patent reads:

> A vaccine comprising (a) a defective poxvirus that lacks a function imparted by an essential region of its parental poxvirus, wherein (i) said defective poxvirus comprises a DNA polynucleotide encoding an antigen and said DNA polynucleotide is under transcriptional control of a promoter, and (ii) the function can be complemented by a complementing source; and (b) a pharmaceutically acceptable carrier.

The Administrative Patent Judge (APJ) designated claims 1-19 of the Falkner '212 patent and claims 9,10, 29, and 30 of the Inglis '040 application as corresponding to the interference count.[1] Both parties sought the benefit of earlier-filed applications to establish dates of constructive reduction to practice.[2] The ALJ accorded the Inglis '040

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[1] Inglis's claim 29 is his broadest claim, directed to poxvirus; and claim 30, which depends on claim 29, is a poxvirus vaccine for mammalian subjects. Claim 9 is directed to poxvirus but contains some additional limitations unrelated to the type of virus used; claim 10 depends on claim 9 and is directed to a single species of poxvirus, namely vaccinia virus. Falkner's claims 2-10 depend on claim 1. Falkner claim 10 is directed to a method of producing the vaccine of claim 1, and the remaining method claims depend thereon.

[2] Priority in an interference goes to the first to invent, but a rebuttable presumption exists that the inventors made their inventions in the chronological order of their effective filing dates, namely that the senior party invented first, see 37 C.F.R. § 1.657(a) (2004), and the junior party bears the burden of proving otherwise, see § 1.657(b), such as by proving that she actually reduced the invention to practice before the constructive filing date (priority date) of the senior party, or that she was first to conceive and diligently reduced the invention to practice, starting from a date prior to reduction to practice by the senior party. See 35 U.S.C. § 112(g) (2000). Falkner sought to rely, in part, on an alleged date of conception and beginning of reasonable diligence: April 27, 1994.

application (filed June 2, 1995) the benefit of several earlier-filed applications, dating back to September 25, 1990.[3] Likewise, the APJ accorded the Falkner '212 patent (issued June 23, 1998 from an application filed February 21, 1997) the benefit of earlier-filed applications, but these dated back only to April 29, 1994.[4] Consequently, the APJ designated Inglis as the senior party.

C. Board Decision

The specifications of all of Inglis' earlier applications were similar. Although they focused on herpesvirus vectors, they contained several passages related to poxvirus-based vaccines. Because Falkner believed that these passages did not adequately describe and enable the poxvirus invention, he challenged both Inglis' entitlement to priority as to the count and the patentability of Inglis' corresponding claims. Falkner brought these challenges in three closely-related preliminary motions before the Board.

On September 13, 2004, the "600" rules expired in favor of new rules found at 37 C.F.R. § 41.100 et seq. However, the Board correctly chose to decide the matter under the old rules, given the parties' reliance on them in filing all motions, oppositions, and replies in the case, which were completed before the new rules took effect. See Singh v. Brake, 222 F.3d 1362, 1371 (Fed. Cir. 2000) (applying a new procedural rule if and only if it did not affect the parties' reliance interests).

[3] The Inglis priority applications were U.S. Application Serial No. 08/384,963 ("the Inglis '963 application"), filed February 7, 1995; U.S. Application Serial No. 08/030,073 ("the Inglis '073 application"), filed May 20, 1993; WO/92/05263, PCT/GB91/01632 ("the Inglis PCT application"), filed September 23, 1991, published in English on April 2, 1992; GB 9104903.1 ("the Inglis 1991 British application"), filed March 8, 1991; and GB 9020799.4 ("the Inglis 1990 British application"), filed September 25, 1990. The Inglis '040 application is a continuation in part of the '963 application, which was in turn a continuation of the Inglis '073 application. The '073 application corresponded to the Inglis PCT application. The Inglis PCT application claimed priority to, and was essentially identical to, the Inglis 1990 and 1991 British applications.

[4] The Falkner priority applications were U.S. Application Serial No. 08/616,313 ("the Falkner '313 application") filed March 14, 1996; and U.S. application Serial No. 08/235,392 ("the Faulkner '392 application"), filed April 29, 1994.

In each, as the moving party, Falkner carried the burden of proof by a preponderance of the evidence. See 37 C.F.R. § 1.637(a); see also Kubota v. Shibuya, 999 F.2d 517, 520 n.2 (Fed. Cir. 1993) (explaining that "[t]he term 'burden of proof' . . . means the burden to establish the proposition at issue by a preponderance of the evidence").

Falkner brought his first preliminary motion pursuant to 37 C.F.R. § 1.633(a),[5] arguing that the claims in Inglis's involved ('040) application that corresponded to the count were unpatentable because they failed to meet the written description requirement of 35 U.S.C. § 112. In support of his argument, he stated, inter alia, that (1) the specification of Inglis's '040 application did not identify any essential genes in poxvirus or describe the inactivation of such genes, (2) vaccines based on vaccinia (a type of poxvirus) had not yet been produced, and (3) the bulk of the Inglis specification was directed not to poxviruses but to herpesviruses. The Board denied Falkner's motion, based in part on his failure to address the perceived shortcomings of the '040 claims in light of the specification.

Second, Falkner moved pursuant to 37 C.F.R. §§ 1.633(g) & 1.637(g) to deny Inglis the priority benefit of his earlier applications, arguing that they did not sufficiently

[5] On September 13, 2004, the "600" rules expired in favor of new rules found at 37 C.F.R. § 41.100 et seq. However, the Board correctly decided the matter under the old rules, given the parties' reliance on them in filing all motions, oppositions, and replies in the case, which were completed before the new rules took effect. See Singh v. Brake, 222 F.3d 1362, 1371 (Fed. Cir. 2000) (applying a new procedural rule if and only if it did not affect the parties' reliance interests); see also Brown v. Barbacid, 436 F.3d 1376, 1379 n.1 (Fed. Cir. 2006) (holding that the Board did not err in applying the old rules "under which this case was decided").

describe and enable the claims in question.[6] Falkner argued that without the benefit of these applications Inglis would be unable to establish constructive reduction to practice earlier than Falkner. Falkner would win priority as to the count, and Inglis' corresponding claims would be unpatentable. In support of his motion, Falkner alleged deficiencies in Inglis' benefit specifications similar to those raised in his first motion. The Board carefully articulated the legal standard, correctly explaining that "benefit with respect to priority in an interference is granted with respect to counts not claims" and that "[a]ll that is necessary for a party to be entitled to benefit of an earlier filed application for priority purposes is compliance with 35 U.S.C. § 112 with respect to at least one embodiment within the scope of the count." Board Op. at 7 (citing Hunt v. Treppschuh, 523 F.2d 1386, 1389 (CCPA 1975) (holding that where a "parent application is relied upon as a prior constructive reduction to practice[,] . . . . the § 112, first paragraph requirements need only be met for an embodiment within the count")). After careful review of the record, the Board held that Falkner had failed to meet his burden of proof.

Third, Falkner moved for judgment pursuant to 37 C.F.R. § 1.633(a) that the claims in Inglis' involved ('040) application that corresponded to the count were anticipated and therefore unpatentable. He argued that because Inglis' earlier applications had failed to adequately describe and enable the full scope of his current claims, the current claims could not be accorded the benefit of 35 U.S.C. § 120 for the

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[6] Falkner did not argue lack of enablement with respect to the Inglis '963 patent because he believed that the teachings of the Falkner '392 patent, filed in 1994, would have enabled the subsequent '963 patent.

purpose of antedating patent-defeating prior art.[7] The Board explained that 35 U.S.C. §§ 119 & 120 require benefit applications to comply with § 112, first paragraph, with respect to the full scope of what a party now claims, rather than with respect to merely one embodiment within the scope of the interference count. After carefully considering the written description and enablement issues, the Board denied the motion. As a result of the denial of Falkner's several motions, Inglis remained the senior party, and the Board ordered judgment as to the subject matter of the count in favor of Inglis.

D. Issue and Standard of Review

On appeal, Falkner essentially reiterates the arguments that he made before the Board. While we recognize that each of these three arguments is distinct, they are nonetheless all related, and under the facts of this particular case, we need only to resolve the following common issue: whether the Inglis benefit applications adequately describe and enable a poxvirus-based vaccine. Falkner also argues that the Board committed other errors, such as initially designating Inglis as the senior party and failing to afford Falkner an opportunity for briefing prior to making this designation. These arguments lack merit, and we shall not further discuss them. We turn, therefore, to the central issues in this case: written description and enablement.

Written description is a question of fact, judged from the perspective of one of ordinary skill in the art as of the relevant filing date. See Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991). Enablement is a question of law involving underlying factual inquiries. See Genentech, Inc. v. Novo Nordisk A/S, 108 F.3d 1361,

[7] Here, Falkner points to his own U.S. Pat. No. 5,766,882 ("the '882 patent'), issued in March 1995, as the patent-defeating prior art.

1365 (Fed. Cir. 1997); see also In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988) (holding that whether undue experimentation is required is a "conclusion reached by weighing many factual considerations. . . . includ[ing] (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.").

This court applies the standards of the Administrative Procedure Act ("APA") in reviewing decisions of the Board. See Dickinson v. Zurko, 527 U.S. 150, 152 (1999) (holding that 5 U.S.C. § 706 governs our review of PTO appeals). Accordingly, we will set aside actions of the Board if they are arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law, and we set aside factual findings that are unsupported by substantial evidence. See In re McDaniel, 293 F.3d 1379, 1382 (Fed. Cir. 2002) (citing 5 U.S.C. § 706); see also In re Sullivan, 362 F.3d 1324, 1326 (Fed. Cir. 2004) (substantial evidence review of factual findings). We review questions of law de novo. See Rapoport v. Dement, 254 F.3d 1053, 1058 (Fed. Cir. 2001).

Substantial evidence is defined as that which a reasonable person might accept as adequate to support a conclusion. See In re Zurko, 258 F.3d 1379, 1384 (Fed. Cir. 2001). It requires an examination of the record as a whole, taking into account both the evidence that justifies and detracts from an agency's opinion. See In re Gartside, 203 F.3d 1305, 1312 (Fed. Cir. 2000). An agency decision can be supported by substantial evidence, even where the record will support several reasonable but contradictory conclusions. See id.; see also In re Jolley, 308 F.3d 1317, 1320 (Fed. Cir. 2002).

II. DISCUSSION

A. Contents of the Inglis Priority Applications

The claims that correspond to the count of the interference are directed to a novel type of vaccine that is comprised of a "vector virus" in the poxvirus family. Conceptually, poxviruses are a "subgenus" of viruses that includes the "species" vaccinia. All of the prior Falkner applications described poxvirus vaccine vectors in detail, and to the exclusion of other types of vaccine vectors (e.g., herpesvirus vaccine vectors). These applications provided five detailed working examples regarding the preparation and use of vaccines from defective poxviruses. They also described the use of a particular species of poxvirus vaccine vector, namely vaccinia virus.

In contrast, the Inglis applications described vaccine vectors in general, and then focused on the subgenus of herpesviruses, for which they provided a detailed example. Nevertheless, at least three passages discussed the poxvirus invention and specifically mentioned "vaccinia virus."[8] For example, after introducing the concept of vaccine vectors, the specification states that "[t]ypically members of the pox virus family, e.g. vaccinia virus, are used as vaccine vectors."[9] The specification later discusses the deletion of essential genes from vaccine vector genomes, noting that the "invention can

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[8] We recognize that the Inglis applications do not describe any actual reduction to practice of a poxvirus vaccine. See Carroll Declaration (stating that the '040 application did not contain any discussion of the "actual creation of the recited 'mutant poxvirus'" and that the application in fact stated "that a vaccinia virus with a deletion in an essential gene had not been produced."). As we discuss below, however, an actual reduction to practice is unnecessary to satisfy the written description requirement.

[9] Because of the substantial similarity in the specifications of all of the Inglis benefit applications, we shall refer in this opinion to representative passages from the earliest of the applications, the Inglis 1990 British application.

be applied to any virus where one or more essential gene(s) can be identified and deleted from or inactivated within the virus genome" (emphasis added). Moreover, it provides that "the virus may comprise an orthopox virus, for example, vaccinia virus, which may comprise a heterologous sequence encoding an immunogen derived from a pathogen." Finally, it reads:

> For example vaccinia virus, a poxvirus, can carry and express genes from various pathogens, and it has been demonstrated that these form effective vaccines when used in animal experimental systems. The potential for use in humans is vast, but because of the known side effects associated with the widespread use of vaccinia as a vaccine against smallpox, there is reluctance to use an unmodified vaccine in humans. There have been attempts to attenuate vaccinia virus by deleting non-essential genes such as the vaccinia growth factor gene. . . However, such attenuated viruses can still replicate in vivo, albeit at a reduced level. No vaccinia virus with a deletion in an essential gene has yet been produced, but such a virus, deleted in an essential gene as described above, with its complementing cell for growth, would provide a safer version of this vaccine.

The application provides a detailed example of an embodiment that comprised not a poxvirus, but a herpesvirus, including the identity of the deleted essential sequences therein. Nevertheless, for the reasons discussed below, we find no error in the Board's determinations on the adequacy of written description and enablement in the various Inglis disclosures.

B. Enablement

Because the adequacy of the disclosure is judged from the perspective of one of ordinary skill in the art, we start our review of the Board's decision by noting that the parties stipulated to a high level of skill in the art. They defined the skilled artisan as having 5-10 years experience creating recombinant poxvirus, as being familiar with the poxvirus literature, the use of poxvirus as a vector for the expression of heterologous genes, and having the "needed technical skill to practice the experimentation described

in the scientific literature relating to recombinant virus, including poxvirus." The Board agreed with the parties' stipulation as to level of skill.

The Board did not err in finding Inglis' claims to be enabled as a matter of law, in light of its articulated underlying factual findings. In support of its conclusion, it noted that "there is extensive disclosure of the selection of an essential gene, its deletion or inactivation and the production of a mutated virus with said deleted or inactivated gene, albeit for herpesvirus." Moreover, because the differences between the herpesviruses and poxviruses were well known, this would have aided the person of ordinary skill in the art in her application of the lessons of the herpesvirus example in the construction of poxvirus vaccines. The Board observed that "the mere fact that the experimentation may have been difficult and time consuming does not mandate a conclusion that such experimentation would have been considered to be 'undue' in this art. Indeed, great expenditures of time and effort were ordinary in the field of vaccine preparation." Thus, the Board found the Inglis applications to be enabling.

Reviewing the Board's legal conclusion of enablement, as based on its underlying findings of fact, we cannot say that the Board erred. With respect to a skilled artisan's ability to identify "essential" poxvirus genes, as discussed below we note that there was undisputed testimony that as of the time of filing of the earliest Inglis application publications in professional journals had disclosed the DNA sequence of the poxvirus genome along with the locations of the "essential regions." The person of ordinary skill in the art would clearly have possessed such knowledge, and given the ready accessibility of the journals, the absence of incorporation by reference is not problematic. Indeed, "[a] patent need not teach, and preferably omits, what is well

known in the art." Spectra-Physics, Inc. v. Coherent, Inc., 827 F.2d 1524, 1534 (Fed. Cir. 1987).

C. Written Description

On appeal to this court, Falkner essentially reargues the positions on written description that he took before the Board. Although the Board erred in its articulation of the written description standard, that error is harmless. The Board held that "an actual possession standard is not required." (emphasis added). But our precedent clearly establishes that "[t]he applicant must . . . convey to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention." Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991). Nonetheless, we conclude there is no need for remand because the undisputed testimony supports the Board's ultimate conclusion.

As noted above, the Board found several passages in the Inglis '040 application (and in the benefit applications) that were directed to poxvirus. No length requirement exists for a disclosure to adequately describe an invention. See In re Hayes Microcomputer Prods., Inc. Patent Litig., 982 F.2d 1527, 1534 (Fed. Cir. 1992) ("[T]he adequacy of the description of an invention depends on its content in relation to the particular invention, not its length."). Furthermore, the testimony of Falkner's expert, Dr. Boursnell, established that the articles describing essential genes for poxvirus were well-known in the art. Dr. Boursnell testified that "the skilled person would have been readily able to choose an essential vaccinia gene" based on references that have been publicly available since 1990. The testimony of Inglis' expert, Dr. Carroll, did not refute this claim.

The parties also dispute several aspects of our law of written description, which we now address. We conclude that the Board applied correct law. Specifically, we hold, in accordance with our prior case law, that (1) examples are not necessary to support the adequacy of a written description (2) the written description standard may be met (as it is here) even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure.

1. Examples Are Not Required

First, it is clear that the absence of examples involving poxviruses in the Inglis applications does not render the written description inadequate. As we explained in LizardTech, Inc. v. Earth Resource Mapping, PTY, Inc.:

> A claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language. That is because the patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before. Placed in that context, it is unnecessary to spell out every detail of the invention in the specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention and to enable such a person to make and use the invention without undue experimentation.

424 F.3d 1336, 1345 (Fed. Cir. 2005) (citing Union Oil Co. v. Atl. Richfield Co., 208 F.3d 989, 997 (Fed. Cir. 2000); In re GPAC Inc., 57 F.3d 1573, 1579 (Fed. Cir. 1995)).

2. Actual Reduction to Practice Is Not Required

As we explained in Capon v. Eshhar, "[t]he 'written description' requirement implements the principle that a patent must describe the technology that is sought to be patented; the requirement serves both to satisfy the inventor's obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the

patentee was in possession of the invention that is claimed." 418 F.3d 1349, 1357 (Fed. Cir. 2005). The Board was correct, however, not to view as dispositive that Inglis had not actually produced a poxvirus vaccine,[10] because an actual reduction to practice is not required for written description.[11] See Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 926 (Fed. Cir. 2004) ("We of course do not mean to suggest that the written description requirement can be satisfied only by providing a description of an actual reduction to practice. Constructive reduction to practice is an established method of disclosure . . . ."). Rochester, moreover, is consistent with Supreme Court precedent. In the context of interpreting 35 U.S.C. § 102(b), the Court held that "[t]he word 'invention' must refer to a concept that is complete, rather than merely one that is 'substantially complete.'" Pfaff v. Wells Elecs., 525 U.S. 55, 66 (1998). It then proceeded to make clear that although "reduction to practice ordinarily provides the best evidence that an invention is complete. . . . it does not follow that proof of reduction

[10] The Inglis specifications stated that "[n]o vaccinia virus with a deletion in an essential gene has yet been produced, but such a virus, deleted in an essential gene as described above, with its complementing cell for growth, would provide a safer version of this vaccine."

[11] The Board believed that Falkner's expert, Dr. Carroll, had premised his opinions on the misunderstanding that actual reduction to practice was required to prove written description, and it discredited his expert opinion.

to practice is necessary in every case." Id. (emphasis added).[12] Thus, to the extent that written description requires a showing of "possession of the invention," Capon, 418 F.3d at 1357 (emphasis added), Pfaff makes clear that an invention can be "complete" even where an actual reduction to practice is absent.[13] The logical predicate of "possession" is, of course, "completeness."

3. Recitation of Known Structure Is Not Required

Falkner argues, inter alia, that the Inglis specifications do not adequately describe the poxvirus invention, in light of Eli Lilly, because they do not describe the "essential regions" of any poxvirus. 119 F.3d 1559. We note, in addition, that Inglis did not attempt to incorporate by reference any literature that described the DNA sequence of the poxvirus genome and the locations of the "essential regions." However, it is the binding precedent of this court that Eli Lilly does not set forth a per se rule that whenever a claim limitation is directed to a macromolecular sequence, the specification must always recite the gene or sequence, regardless of whether it is known in the prior art. See Capon, 418 F.3d at 1357 ("None of the cases to which the Board attributes the requirement of total DNA re-analysis, i.e., Regents v. Lilly, Fiers v. Revel, Amgen, or

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[12] Similarly, this court has carefully explained the relationship between written description and possession, explaining that a showing of possession is not necessarily sufficient to demonstrate the adequacy of written description. See, e.g., Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 1330 (Fed. Cir. 2002) ("[P]roof of a reduction to practice, absent an adequate description in the specification of what is reduced to practice, does not serve to describe or identify the invention for purposes of § 112, P 1. As with 'possession,' proof of a reduction to practice may show priority of invention or allow one to antedate a reference, but it does not by itself provide a written description in the patent specification.").

[13] In contrast to reduction to practice, conception is a prerequisite to an adequate written description. See Fiers v. Sugano, 984 F.2d 1164, 1171 (Fed. Cir. 1993) ("[O]ne cannot describe what one has not conceived.").

Enzo Biochem, require a re-description of what was already known."). Thus, "[w]hen the prior art includes the nucleotide information, precedent does not set a per se rule that the information must be determined afresh." Id. at 1358. Rather, we explained that:

> The descriptive text needed to meet these requirements varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence. The law must be applied to each invention that enters the patent process, for each patented advance is novel in relation to the state of the science. Since the law is applied to each invention in view of the state of relevant knowledge, its application will vary with differences in the state of knowledge in the field and differences in the predictability of the science.

Id. at 1357.

Indeed, a requirement that patentees recite known DNA structures, if one existed, would serve no goal of the written description requirement. It would neither enforce the quid pro quo between the patentee and the public by forcing the disclosure of new information, nor would it be necessary to demonstrate to a person of ordinary skill in the art that the patentee was in possession of the claimed invention. As we stated in Capon, "[t]he 'written description' requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution." Id. at 1358. Indeed, the forced recitation of known sequences in patent disclosures would only add unnecessary bulk to the specification. Accordingly we hold that where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences (here "essential genes"), satisfaction of the written description requirement does not

require either the recitation or incorporation by reference[14] (where permitted) of such genes and sequences.

In conclusion, having reviewed the decision of the Board, we can discern no error in its conclusion that the disclosures relied upon by Inglis for priority purposes adequately described and enabled the invention directed to poxvirus, there being substantial evidence to support these findings. Consequently, we hold that the Board's award of priority to Inglis was proper.

AFFIRMED

No costs.

[14] Here, the patentee did not attempt incorporation by reference. Where, of course, certain material that is not present in the specification is deemed nonessential to the satisfaction of the written description requirement, the issue of proper incorporation by reference vel non is irrelevant.